II. REMARKS

A. Status of the Claims

Claims 1, 2, 31-33, 35-51 and 60 were pending in the case at the time of the Office Action, with claims 5, 10-28, and 34 having been previously withdrawn from consideration. Claims 1, 2, 5, and 60 have been amended in the Amendment set forth herein. Claims 3-4, 6-13, 18-22, 29-30, and 52-59 have been canceled without prejudice or disclaimer. No new claims have been added. Support for the amendments of the claims can be found generally throughout the specification, such as in the claims as originally filed. Thus, claims 1, 2, 31-33, 35-51, and 60 are currently under consideration.

B. Amendment to the Specification

Applicants have amended the claims to omit certain subject matter invented by Jerry L. Bryant. These amendments are made without prejudice or disclaimer. In view of these amendments to the claims, Applicants, in accordance with 37 C.F.R. §1.48(b) request that the inventorship be corrected, as Jerry Bryant's invention is no longer being claimed in the present nonprovisional application. Applicants reserve the right to prosecute this subject matter in a divisional or continuation application. As set forth above, the Commissioner is authorized to deduct the required processing fee set forth in 37 C.F.R. §1.17(i) from Fulbright & Jaworski Deposit Account No. 50-1212/UTSC:841US.

C. The Double Patenting Rejections Are Overcome

1. The Nonstatutory Obviousness-Type Double Patenting Rejections Are Overcome

Claims 1, 2, and 31-33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent 6,692,724. Claims 35-41

are rejected on the ground of obviousness-type double patenting as being unpatentable over claims 1-5 and 7 of U.S. Patent 7,067,111. Applicants respectfully traverse.

It is respectfully submitted that neither of the cited patents teaches or suggests any of the targeting ligands of the claimed invention. Without a teaching or suggestion as to each limitation of the claimed invention, the Examiner has failed to establish a *prima facie* case of obviousness. Should this be the only remaining issue, Applicants will readdress whether or not to file a terminal disclaimer.

2. The Provisional Rejections Based On Nonstatutory Obviousness-Type Double Patenting Will Be Addressed When The Rejections Are No Longer Provisional

Claim 38 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 52-73 of copending application No. 10/672,763. Claims 42-51 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42-50 and 74-81 of copending application 11/405,334. Applicants understand that these rejections are only provisional. Applicants respectfully traverse these provisional rejections. It is respectfully submitted that in view of the amendment set forth herein, none of the targeting ligands is of overlapping scope with those set forth in application 10/672,763 or application 11/405,334.

D. The Claim Rejections Under 35 U.S.C. §112, Second Paragraph, Are Overcome

Claim 60 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, this claim is said to be indefinite for depending from claim 6, which has been previously canceled. Applicants respectfully traverse.

Claim 60 has been amended to depend from claim 1 rather than claim 6. Therefore, this rejection is overcome.

E. The Claim Rejections Under 35 U.S.C. §103 Are Overcome

Claims 1, 2, 31-33, 35-51, and 60 are rejected under 35 U.S.C. §103(a) as being unpatentable over Iyer *et al.* (J. Nucl. Med., 2001, 42, p. 96-104; hereinafter "Iyer") in view of WO 01/91807. Applicants respectfully traverse.

1. WO 01/91807 is Not Prior Art

Applicants note as an initial matter than WO 01/91807 has a publication date of December 6, 2001 and the present application has a priority date of November 7, 2002. Therefore, because WO 01/91807 was published less than one year before the priority date of the present application, it is not prior art under 35 U.S.C. §102(b), and therefore Applicants are not barred from submitting declaratory evidence to overcome WO 01/91807 as prior art. See *MPEP* §706.02, §716,10, §2136, 37 C.F.R. §1.131-132. The basis for using this international application as prior art include §102(a) and §102(g).

To overcome WO 01/91807 as prior art under 35 U.S.C. §102(a) and 35 U.S.C. §102(g), Applicants herein submit a declaration of David J. Yang, Dong Fang Yu, Chun-Wei Liu, and E. Edmund Kim, who are listed as inventors on WO 01/91807 (Exhibit 1). These individuals have declared that certain subject matter disclosed in WO 01/91807 was invented jointly by David J. Yang and Don Fang Yu, and not by Chun-Wei Liu or E. Edmund Kim. David J. Yang and Dong Fang Yu are two of the inventors of the present application. Per paragraph 2 of the declaration, this subject matter includes, but is not necessarily limited, to the following subject matter:

- The conjugation of an N_2S_2 chelate (such as ethylenedicysteine) to a targeting ligand, including those targeting ligands set forth in WO 01/91807, such as acylovir and ganciclovir.

- The conjugation of a targeting ligand to an N_2S_2 chelate via an amino or hydroxy group of the targeting ligand, by use of a linker, and chemical modification of targeting agents with amino groups for purposes of conjugation of the targeting ligand to the N_2S_2 chelate.
- Radiolabelling of an N_2S_2 chelate with a targeting ligand, including labelling with 99mTc.

David J. Yang and Don Fang Yu closely collaborated with each other and worked in the same laboratory at M.D. Anderson Cancer Center at the time they invented the subject matter set forth above. See Exhibit 1, paragraph 3.

Thus, Applicants have herein set forth evidence that the relevant parts of WO 01/91807 that have been relied upon by the Examiner in setting forth this rejection originated with and were invented solely by two of the inventors of the claims currently under examination (*i.e.*, the claimed subject matter). Thus, WO 01/91807 is not available as prior art under either §102(a)/§103(a) or §102(g)/§103(a).

Further, to the extent that any U.S. patent or patent application related to WO 01/91087 is being considered as prior art under §102(e)/§103(a), Applicants note that the presently claimed invention and the invention set forth in WO 01/91087 were subject to a common obligation of assignment to the Board of Regents, the University of Texas System, at the time the present invention was made. Therefore, such a U.S. patent or patent application would not be prior art under 35 U.S.C. §103(a).

In view of the foregoing, WO 01/91087 is not prior art. In the absence of WO 01/91087, Iyer fails to render the claimed invention obvious because it provides no teaching or suggestion

to conjugate any of the targeting ligands set forth in the claims to an N_2S_2 chelate, or any method of imaging using such a conjugate. In the absence of this teaching or suggestion, there can be no *prima facie* case of obviousness.

2. Even if WO 01/91087 Was Available As Prior Art Under 35 U.S.C. §103(a), There Would Still Be No *Prima Facie* Case of Obviousness

Even if WO 01/91087 was available as prior art under 35 U.S.C. §103(a), there would still be no prima facie case of obviousness because Iyer in view of WO 01/91087 fails to provide any suggestion or motivation to lead to the claimed invention.

Iyer concerns 18F-labeled penciclovir as a probe for imaging HSV1-thymidine kinase reporter gene expression. Iyer appears to focus solely on probes with single atom radiolabels, including ^{18}I, ^{124}I, ^{3}H labeled chemical substrates. Nothing in Iyer teaches or suggests substituting 18F with a chemical moiety, such as a radiolabeled N2S2 chelate, for imaging. In fact, Iyer suggests that such a substitution would not result in such a probe not being an effective reporter, and thus seems to teach away from the claimed invention. For example, on page 97, second full paragraph, Iyer teaches that slight structural variations have a significant effect on biological activity. In particular, Iyer teaches that "the lack of an ether oxygen in the side chain of PCT has a significant effect on its biological properties," even though PCT is "structurally similar to GCV." Page 97, second paragraph.

Further, WO 01/91087 does not provide the missing teaching or suggestion to modify the probes of Iyer by conjugating aminopenciclovir or penciclovir to an N2S2 chelate. WO 01/91087 provides no teaching or suggestion concerning penciclovir or aminopenciclovir, or any of the targeting ligands of the pending claims. The Examiner appears to argue that the disclosure in WO 01/91087 concerning ganciclovir and acyclovir somehow teaches one of ordinary skill in the art to substitute these targeting ligands with penciclovir. However, Iyer teaches distinctions

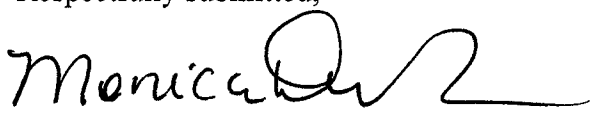
between ganciclovir and penciclovir, noting that the lack of an ether oxygen in the side chain of penciclovir has "a significant effect on biological activity." Page 97, paragraph 2. Thus, one of ordinary skill in the art, when presented with these references, would not be motivated to prepare a radiolabeled N2S2 targeting ligand conjugate for imaging applications.

In view of the foregoing, claims 1, 2, 31-33, and 35-51 are not unpatentable under 35 U.S.C. §103(a) based on Iyer in view of Yang. Therefore, it is respectfully requested that this rejection should be withdrawn.

F. Conclusion

In view of the foregoing, it is respectfully submitted that each of the pending claims is in condition for allowance, and a Notice of Allowance is earnestly solicited. The Examiner is invited to contact the undersigned attorney at (512) 536-5639 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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Date: April 30, 2008

EXHIBIT 1

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Yang, *et al.*

Serial No.: 10/732,919

Filed: December 10, 2003

For: N2S2 Chelate-Targeting Ligand Conjugates

Confirmation No. 7351

Group Art Unit: 1618

Examiner: Schlientz, Leah H.

Atty. Dkt. No.: UTSC:841US

CERTIFICATE OF ELECTRONIC TRANSMISSION
37 C.F.R. § 1.8

I hereby certify that this correspondence is being electronically filed with the United States Patent and Trademark Office via EFS-Web on the date below.

4/30/08 — Monica A. De La Paz
Date

DECLARATION OF DAVID J. YANG, DONG FANG YU, CHUN-WEI LIU, AND E. EDMUND KIM

We, David J. Yang, Dong Fang Yu, Chun-Wei Liu, and E. Edmund Kim, do declare that:

1. We are listed as co-inventors of WO 01/91807, entitled "Ethylenedicysteine (EC)-Drug Conjugates, Compositions and Methods for Tissue Specific Disease Imaging" (international publication date December 6, 2001).

2. Certain subject matter disclosed in WO 01/91807 was invented jointly by David J. Yang and Don Fang Yu, and not Chun-Wei Liu or E. Edmund Kim. This subject matter includes, but is not necessarily limited, to the following:

    - The conjugation of an N_2S_2 chelate (such as ethylenedicysteine) to a targeting ligand, including those targeting ligands set forth in WO 01/91807, such as acylovir and ganciclovir.

- The conjugation of a targeting ligand to an N_2S_2 chelate via an amino or hydroxy group of the targeting ligand, by use of a linker, and chemical modification of targeting agents with amino groups for purposes of conjugation of the targeting ligand to the N_2S_2 chelate.
- Radiolabelling of an N_2S_2 chelate with a targeting ligand, including labelling with 99mTc

3. David J. Yang and Don Fang Yu closely collaborated with each other and worked in the same laboratory at M.D. Anderson Cancer Center at the time they invented the subject matter set forth in paragraph 2 above.

4. We hereby declare that all statements made by our own knowledge are true and all statements made on information and belief are believed to be true and further that statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment under § 100 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issued thereon.

David J. Yang — 4/25/2008
David J. Yang — Date

Dong Fang Yu — 4/25/08
Dong Fang Yu — Date

Chun-Wei Liu — Date

E. Edmund Kim — 4/28/08
E. Edmund Kim — Date

PATENT

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Monica A. De La Paz

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David J. Yang	Date
Dong Fang Yu	Date
Chun-Wei Liu	4/25/2008 Date
E. Edmund Kim	Date